Toxicological Profile for

CADMIUM
(Update)

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

TOXICOLOGICAL PROFILE FOR CADMIUM

Prepared by:

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July 1999

eat foods that contain enough iron or other nutrients, you are likely to take up more cadmium from your food than usual. Virtually no cadmium enters your body through your skin.

Most of the cadmium that enters your body goes to your kidney and liver and can remain there for many years. A small portion of the cadmium that enters your body leaves slowly in urine and feces. Your body can change most cadmium to a form that is not harmful, but too much cadmium can overload the ability of your liver and kidney to change the cadmium to a harmless form, and the harmful form may damage your health.

More information on how cadmium enters and leaves the body is found in Chapter 2.

1.5 HOW CAN CADMIUM AFFECT MY HEALTH?

The potential for cadmium to harm your health depends upon the form of cadmium present, the amount taken into your body, and whether the cadmium is eaten or breathed. There are no known good effects from taking in cadmium. Breathing air with very high levels of cadmium can severely damage the lungs and may cause death. Breathing air with lower levels of cadmium over long periods of time (for years) results in a build-up of cadmium in the kidney, and if sufficiently high, may result in kidney disease. Other effects that may occur after breathing cadmium for a long time are lung damage and fragile bones.

To protect the public from the harmful effects of toxic chemicals and to find ways to treat people who have been harmed, scientists use many tests.

One way to see if a chemical will hurt people is to learn how the chemical is absorbed, used, and released by the body; for some chemicals, animal testing may be necessary. Animal testing may also be used to identify health effects such as cancer or birth defects. Without laboratory animals, scientists would lose a basic method to get information needed to make wise decisions to protect public health. Scientists have the responsibility to treat research animals with care and

1: Environ Health Perspect 1979 Apr;29:95-104

Nutritional influences on metal toxicity: cadmium as a model toxic element.

Fox MR.

The nutrient quality of the diet has been shown repeatedly to be a significant factor in modifying the response of man and animals to toxic element exposure. Deficiencies of several essential nutrients have been shown to exacerbate the effects of cadmium and supplements of such nutrients have been shown to ameliorate the toxicity. Thus the effects of exposure to a toxic element, such as cadmium, may vary, depending on interactions with other elements which are present in the diet in different concentrations.

PMID: 510248 [PubMed - indexed for MEDLINE]

1: Rev Environ Contam Toxicol 1991;119:47-145

Small mammals as monitors of environmental contaminants.

Talmage SS, Walton BT.

Health and Safety Research Division, Oak Ridge National Laboratory, TN 37831-6050.

The merit of using small mammals as monitors of environmental contaminants was assessed using data from the published literature. Information was located on 35 species of small mammals from 7 families used to monitor heavy metals, radionuclides, and organic chemicals at mine sites, industrial areas, hazardous and radioactive waste disposal sites, and agricultural and forested land. To document foodchain transfer of chemicals concentrations in soil, vegetation, and invertebrates, where available, were included. The most commonly trapped North American species were Peromyscus leucopus, Blarina brevicauda, and Microtus pennsylvanicus. In these species, exposure to chemicals was determined from tissue residue analyses, biochemical assays, and cytogenetic assays. Where enough information was available, suitable target tissues, or biological assays for specific chemicals were noted. In general, there was a relationship between concentrations of contaminants in the soil or food, and concentrations in target tissues of several species. This relationship was most obvious for the nonessential heavy metals, cadmium, lead, and mercury and for fluoride. Kidney was the single best tissue for residue analyses of inorganic contaminants. However, bone should be the tissue of choice for both lead and fluorine. Exposure to lead was also successfully documented using biochemical and histopathological endpoints. Bone was the tissue of choice for exposure to 90Sr, whereas muscle was an appropriate tissue for 137Cs. For organic contaminants, exposure endpoints depended on the chemical(s) of concern. Liver and whole-body residue analyses, as well as enzyme changes, organ histology, genotoxicity, and, in one case, population dynamics, were successfully used to document exposure to these contaminants. Based on information in these studies, each species' suitability as a monitor for a specific contaminant or type of contaminant was evaluated and subsequently ranked. A relationship between contaminant exposure and trophic level emerged. Insectivores (shrews) had the highest

levels of contaminants, followed by omnivores (cricetid mice) with intermediate levels, and herbivores (voles) with the lowest levels. A substantial number of these biomonitoring studies using small mammals collectively point to the importance of food habits and habitat of small mammals, and their availability and abundance as factors that should influence species selection for monitoring studies. The type of contaminants under consideration as well as the appropriateness of the endpoints selected are important factors to consider when deciding whether or not to include small mammals in biomonitoring studies.

Publication Types:

- Review
- Review, Academic

PMID: 1992495 [PubMed - indexed for MEDLINE]

1: Toxicol Appl Pharmacol 1990 Sep 15;105(3):413-21

Efflux of endogenous zinc liberated from metallothionein and alcohol dehydrogenase in the liver by replacement with cadmium.

Suzuki KT, Kawahara S, Sunaga H, Shimojo N.

National Institute for Environmental Studies, Ibaraki, Japan.

Efflux of endogenous zinc (Zn) from the liver was examined to aid elucidation of the mechanisms of the discriminative uptake between the essential heavy metal Zn and the nonessential heavy metal cadmium (Cd). Cd was injected intravenously into rats with or without pretreatment of a small dose of Cd 6 or 24 hr earlier. The concentration of Zn in the whole liver decreased with time after Cd injection and the extent of the decrease was more apparent in the liver that contained the Zn bound to metallothionein (MT) by pretreatment. Time course curves of Cd and Zn in liver supernatants were identical to those of the corresponding whole livers, indicating that the changes observed in the whole livers were due to the changes in the supernatants. Distribution profiles of Cd and Zn by gel filtration chromatography indicated that Cd replaced Zn bound to both alcohol dehydrogenase (ADH) and MT. The decrease of Zn in the liver caused by Cd injection was explained by the efflux of the Zn liberated from ADH and MT, which suggests that efflux of Zn ions but not Cd ions occurs from the liver. The results are discussed from the viewpoint of discriminative uptake between Cd and Zn by the liver.

PMID: 2237916 [PubMed - indexed for MEDLINE]

1: Food Addit Contam 1990 Mar-Apr;7(2):207-21

Dietary intakes of some essential and non-essential trace elements, nitrate, nitrite and N-nitrosamines, by Dutch adults: estimated via a 24-hour duplicate portion study.

Ellen G, Egmond E, Van Loon JW, Sahertian ET, Tolsma K.

National Institute of Public Health and Environmental Protection, Bilthoven The Netherlands.

Duplicate portions of 24-hour diets of 110 adults have been analyzed for aluminium, cadmium, copper, lead, manganese, mercury, zinc, nitrate, nitrite and volatile N-nitrosamines. The mean daily intake of copper (1.2 mg) is only about 50% of recommended values; mean daily intakes for manganese (3.3 mg) and zinc (8.4 mg) are adequate and marginal respectively with respect to recommended amounts. For the non-essential elements Al, Cd, Hg and Pb, mean daily intakes of 3.1 mg, 0.01 mg, 0.002 mg and 0.034 mg were found, respectively. For Cd this amounts to 17% of the acceptable daily amount, for Al, Hg and Pb 5%, 5% and 8%, respectively. Since 1976-1978 the dietary intake of lead has been reduced by a factor three; for the other six elements daily dietary intakes are almost the same as in 1976-1978 Average nitrate intake was 52 mg NO3-/day, about 25% of the ADI. Only 16 diets contained a measurable amount of nitrite. The highest daily intake (0.7 mg NO2-) is less than 10% of the ADI. Volatile N-nitrosamines were detectable in two duplicate diets (NDMA and NPIP). It is estimated that the daily dietary intake of volatile N-nitrosamines is around 0.1 microgram or less.

PMID: 2354740 [PubMed - indexed for MEDLINE]

1: Am J Clin Nutr 1989 Nov;50(5):1079-83

Selected ultratrace elements in total parenteral nutrition solutions.

Berner YN, Shuler TR, Nielsen FH, Flombaum C, Farkouh SA, Shike M.

Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY 10021.

Ultratrace elements are potentially essential (eg, boron, molybdenum, nickel and vanadium) or toxic (eg, aluminum and cadmium) in humans. Long-term total parenteral nutrition (TPN) patients can inadvertently receive significant amounts of ultratrace elements present as contaminants in TPN solutions. We determined the intake of selected ultratrace elements from a standard TPN solution and compared it with the amount reported to be absorbed from food in normal subjects. Contamination of TPN solutions with ultratrace elements was widespread and variable. The daily intakes of Mo, Ni, V. and Cd from this contamination were comparable to the amounts reported to be absorbed through the gastrointestinal tract in normal subjects Al intake was high; B intake was low, approximately 10% of the amount absorbed by normal subjects. Thus, TPN solutions are contaminated with significant amounts of ultratrace elements. The biological significance of the intravenous infusion of these ultratrace elements is unclear and requires further investigation, particularly in home TPN patients.

PMID: 2510493 [PubMed - indexed for MEDLINE]

1: J Am Coll Nutr 1989 Aug;8(4):285-91 Related Articles, Links

Trace minerals and the kidney: an overview.

Lindeman RD.

Veterans Administration Medical Center, Washington, DC 20422.

The deviations from normal health produced by abnormalities in trace mineral metabolism in patients with renal disease and renal disorders produced by deficiencies or excesses of these trace minerals serve as the focus for this symposium on trace minerals and the kidney. Zinc, the trace mineral of most interest of the nephrologist, and aluminum, the nonessential (toxic) trace element of most interest, are treated in separate reviews. Iron, copper, selenium, and silicon (essential trace elements) and cadmium, lead, mercury, and lithium (nonessential or toxic elements) are covered in this review.

Publication Types:
- Review
- Review Literature

PMID: 2674254 [PubMed - indexed for MEDLINE]

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1: Prog Food Nutr Sci 1987;11(1):55-113 Related Articles, Links

Biological and health implications of toxic heavy metal and essential trace element interactions.

Chowdhury BA, Chandra RK.

Human civilization and a concomitant increase in industrial activity has gradually redistributed many toxic metals from the earth's crust to the environment and increased the possibility of human exposure. Among the various toxic elements, heavy metals cadmium, lead, and mercury are specially prevalent in nature due to their high industrial use. These metals serve no biological function and their presence in tissues reflects contact of the organism with its environment. They are cumulative poison, and are toxic even at low dose. Studies of metabolism and toxicity of these elements have revealed important interactions between them and some essential dietary elements like calcium, zinc, iron, selenium, copper, chromium, and manganese. In general, a deficiency of these essential elements increases toxicity of heavy metals, whereas an excess appears to be protective. While most of the observations are on laboratory animals, limited human data are in agreement with the results of animal experiments. These suggest that the dietary presence of the essential elements may contribute to the protection of man and animal from the effects of heavy metal exposure, while their deficiency may increase toxicity. Appropriate dietary manipulation thus may be valuable in the prevention and treatment of heavy metal toxicity.

Publication Types:
- Review

PMID: 3303135 [PubMed - indexed for MEDLINE]

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1: J Hypertens Suppl 1986 Dec;4(5):S361-3 Related Articles, Links

Lifestyle/environmental factors and blood cadmium levels in hypertensive and normotensive individuals.

Fontana SA, Boulos BM.

Cadmium is a non-essential trace metal presently found at environmental concentration far exceeding its natural occurrence, to which human populations are exposed form diverse sources. Animals exposed chronically to subtoxic cadmium levels develop hypertension, yet human studies are inconclusive. In the present study, the relationship between lifestyle/environment factors and blood cadmium levels was investigated. Black females aged 50-75 years were chosen from university clinics and community settings (30 normotensives and 32 hypertensives). Questionnaires giving environmental, lifestyle and other date were collected. Cadmium blood levels were determined by atomic absorption spectophotometry; and results indicated a high degree of precision and accuracy for the cadmium analytical technique which was used. No significant differences were found in cadmium blood levels between groups.

PMID: 3471910 [PubMed - indexed for MEDLINE]

Display Abstract Show: 20 Sort Send to Text

1: Ann Intern Med 1983 May;98(5 Pt 2):823-7

Trace elements and blood pressure.

Saltman P.

Essential trace elements such as zinc, iron, and copper participate in various enzyme reactions directly related to the regulation of blood pressure and indirectly related to generation of oxidative metabolic energy, alterations in blood lipid levels, and alterations in taste acuity. The toxicological action of several heavy metal ions including cadmium, lead, mercury, and thallium car cause hypertension by affecting hormone metabolism, vasoconstriction, and renal tubular function. We conclude, however, that neither deficiencies of essential elements nor the presence of toxic heavy metals are primary causes of hypertension in our population.

PMID: 6847020 [PubMed - indexed for MEDLINE]

1: Genome 1993 Apr;36(2):255-60

Field performance and heavy metal concentrations of transgenic flue-cured tobacco expressing a mammalian metallothionein-beta-glucuronidase gene fusion.

Brandle JE, Labbe H, Hattori J, Miki BL.

Agriculture Canada, Research Station, Delhi, Ont.

Cadmium (Cd) is a nonessential heavy metal that can cause acute and chronic illness in humans. Some plant species such as tobacco (Nicotiana tabacum L.) tend to accumulate high levels of Cd in leaf tissue, the consumed portion of the plant. Tissue-specific expression of mammalian metallothionein has been suggested as a means of partitioning Cd in nonconsumed portions of transgenic plants. The purpose of the experiment reported here was to evaluate Cd concentration and agronomic performance of four field-grown transgenic tobacco lines harbouring a metallothionein-beta-glucuronidase (MG) gene fusion driven by the constitutive 35S promoter of cauliflower mosaic virus. The trial was grown in a region of Canada known to have high background levels of Cd. The agronomic evaluation showed that some of the transgenic lines were equal to, while others performed more poorly than, the untransformed control for yield, days to flower, and leaf number. Gene expression measured by beta-glucuronidase activity showed that all of the transgenic lines expressed the MG gene in the upper portion of the plant. One line did not express the MG gene in the roots. Cd levels in the leaf tissue of transformed lines were not significantly different from the untransformed control.

PMID: 8514154 [PubMed - indexed for MEDLINE]

1: Biol Trace Elem Res 1994 Jan;40(1):49-57

Concentrations of cadmium, lead, selenium, and zinc in human blood and seminal plasma.

Xu B, Chia SE, Ong CN.

Department of Occupational Epidemiology, Jiangsu Institute of Occupational Medicine, Nanjing, China.

The concentrations of cadmium, lead, selenium, and zinc in blood and seminal plasma were determined in 76 Singapore males. Except for zinc, the concentrations were generally higher in blood than in seminal plasma (cadmium, 1.31 micrograms/L vs 0.61 micrograms/L; lead, 82.6 micrograms/L vs 12.4 micrograms/L, and selenium, 163.6 micrograms/L vs 71.5 micrograms/L). The mean concentration of zinc in seminal plasma was more than 30 times higher than in blood (202 mg/L vs 6.2 mg/L). Significant positive correlations were found between the concentrations in blood and seminal plasma for the two essential trace elements: selenium ($r = 0.45$, $p < 0.001$) and zinc ($r = 0.25$, $p < 0.05$). However, no relationships were found between the concentrations in blood and seminal plasma for two toxic metals (cadmium and lead). Significant inverse correlations were observed between Cd and Zn ($r = -0.40$, $p < 0.01$), and Pb and Se ($r = -0.32$, $p < 0.05$) in blood, whereas significant positive correlations were noted between Cd and Se ($r = 0.45$, $p < 0.01$), Cd and Zn ($r = 0.35$, $p < 0.05$), and Se and Zn ($r = 0.57$, $p < 0.001$) in seminal plasma. The physiological significance of these relationships are also discussed in this paper.

PMID: 7511920 [PubMed - indexed for MEDLINE]

1: Z Lebensm Unters Forsch 1995 Jul;201(1):7-11

The status of trace elements in staple foods. II. Some effects of cereal and potato processing.

Bruggemann J, Kumpulainen J.

Federal Centre for Cereal, Potato and Lipid Research, Detmold, Germany.

The effects of food processing on some cereal and potato products are discussed with respect to the status of 11 trace elements. The influences of milling, bread making and cooking of potatoes on the contents of trace elements are demonstrated. It is shown that these recently obtained results are quite representative for the former federal Republic of Germany (FRG) as compared with results published previously. Average intake levels of undesired elements such as cadmium and lead, as well as of essential elements such as calcium, copper, iron, magnesium, manganese, molybdenum, nickel, selenium and zinc via consumption of cereal and potato products are calculated.

PMID: 7571869 [PubMed - indexed for MEDLINE]

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1: J Am Coll Nutr 1994 Dec;13(6):559-64

The role of vitamin D in toxic metal absorption: a review.

Moon J.

National College of Naturopathic Medicine, Portland Oregon 97216.

Vitamin D increases intestinal calcium and phosphate absorption. Not so well known, however, is that vitamin D stimulates the co-absorption of other essential minerals like magnesium, iron, and zinc; toxic metals including lead, cadmium, aluminum, and cobalt; and radioactive isotopes such as strontium and cesium. Vitamin D may contribute to the pathologies induced by toxic metals by increasing their absorption and retention. Reciprocally, lead, cadmium, aluminum, and strontium interfere with normal vitamin D metabolism by blocking renal synthesis of 1,25-dihydroxyvitamin D. This is the first review of the role of the vitamin D endocrine system in metal toxicology.

Publication Types:
- Review
- Review, Tutorial

PMID: 7706586 [PubMed - indexed for MEDLINE]

1: Biol Trace Elem Res 1994 Fall;43-45:481-7

Trace element contents in food determined by neutron activation analysis and other techniques.

Reis MF, Abdulla M, Parr RM, Chatt A, Dang HS, Machado AA.

INETI-ICEN-DEEN, Sacavem, Portugal.

Advances in analytical methodology and sophisticated instrumentation introduced during the last few decades have not only helped to recognize the presence of a large number of essential and toxic trace elements in biological materials and food stuffs, but also added a new dimension in our understanding of their role in health and disease. In deficiency states, most essential trace elements cause health problems. The trace element problem as a public health issue has a very low priority in developing countries. Daily dietary intake data based on well-conducted studies are limited in many parts of the world. The present authors are in the process of generating data for the intake levels of a number of major and minor inorganic elements both in developed and developing countries. The results so far obtained show wide variations. The intake levels of several elements, including potassium, magnesium, zinc, copper, and selenium, are below the current recommended levels. The concentration of toxic metals, such as aluminum, cadmium, lead, and mercury, are within acceptable limits in most of the diets analyzed.

PMID: 7710864 [PubMed - indexed for MEDLINE]

1: Arch Toxicol 1994;69(2):132-6 Related Articles, Links

Suppression of interleukin-1 beta and tumour necrosis factor-alpha biosynthesis by cadmium in in vitro activated human peripheral blood mononuclear cells.

Theocharis SE, Souliotis VL, Panayiotidis PG.

Department of Experimental Pharmacology, School of Medicine, University of Athens, Greece.

Cadmium is a highly toxic element responsible for acute and chronic toxicity in man. There is evidence that cadmium induces pathophysiological effects by modulating components of the immune system. Cytokines are being increasingly recognized as essential mediators of normal and pathologic immune responses. Cadmium at concentrations varying from 1.0 x 10(-4) to 3.3 x 10(-6) M inhibited the phytohemagglutinin induced production of interleukin-1 beta and tumour necrosis factor-alpha, in in vitro activated human peripheral blood mononuclear cells. The messenger RNA levels of interleukin-1 beta and tumour necrosis factor-alpha were examined during a 24-h culture period, at different time points. The decreased messenger RNA levels at the time points of the maximum expression of interleukin-1 beta and tumour necrosis factor-alpha indicate that cadmium suppresses their production at the transcriptional level.

PMID: 7717862 [PubMed - indexed for MEDLINE]

1: Am J Clin Nutr 1995 Mar;61(3 Suppl):646S-650S

Nutrition and metal toxicity.

Goyer RA.

National Institute of Environmental Health Sciences, Research Triangle Park, NC 27707.

Lead, cadmium, and mercury are toxic metals that are not essential for nutrition. However, the toxic effects of these metals may be mediated or enhanced by interactions or deficiencies of nutritionally essential metals. Lead competes with calcium, inhibiting the release of neurotransmitters, and interferes with the regulation of cell metabolism by binding to second-messenger calcium receptors, blocking calcium transport by calcium channels and calcium-sodium ATP pumps, and by competing for calcium-binding protein sites and uptake by mitochondria. Dietary deficiencies of calcium, iron, and zinc enhance the effects of lead on cognitive and behavioral development. Iron deficiency increases the gastrointestinal absorption of cadmium, and cadmium competes with zinc for binding sites on metallothionein, which is important in the storage and transport of zinc during development. Selenium protects from mercury and methyl mercury toxicity by preventing damage from free radicals or by forming inactive selenium mercury complexes.

Publication Types:
- Review
- Review, Tutorial

PMID: 7879732 [PubMed - indexed for MEDLINE]

1: Med Hypotheses 1994 Jun;42(6):380-4

The cadmium toxicity hypothesis of aging: a possible explanation for the zinc deficiency hypothesis of aging.

Bin QH, Garfinkel D.

Human Province, Ma-Wang-Dui Sanatorium, Chang Sha, PR China.

Although cadmium and zinc have similar chemical properties, they affect living organisms diversely: while zinc is an essential element for growth, development and functioning of all living cells, cadmium is a highly toxic material. Cadmium has an extremely long biological half-life and may be considered a cumulative toxin. It has been shown to have sterilizing, teratogenic and carcinogenic effects and most of these effects could be reduced or even prevented by zinc administration. An increase in cadmium concentration with age has been proven in various species and in different tissues and these facts led some investigators to the assumption that cadmium accumulation might play an important role in senescence. Zinc essentiality and the lack of a reliable index of intracellular zinc status, formed the rationale for the zinc deficiency hypothesis of aging. This hypothesis suggests a gradual time related zinc deficiency occurring in each living cell, making zinc less available for its metalloenzymes. The sum of all deleterious effects resulting from the distorted function of different zinc enzymes, is later manifested as aging processes. When cadmium concentration increases, zinc concentration in various tissues decreases. Cadmium may inhibit zinc activities at many stages, interfering with zinc absorption, distribution to different tissues and transport into cells or into several intracellular structures. Therefore, it is reasonable to assume that a slowly developing cadmium toxicity may result in a gradual time related zinc deficiency.

PMID: 7935085 [PubMed - indexed for MEDLINE]

1: Sci Total Environ 1994 Jan 25;141(1-3):59-73

Some toxic and trace metals in big game hunted in the northern part of Poland in 1987-1991.

Falandysz J.

Department of Chemistry, University of Gdansk, Poland.

Game animal meats (muscle, liver and kidneys) collected from different regions in northern part of Poland in 1987-1991 were analysed for mercury, cadmium, lead, copper, manganese, zinc and iron. Toxic mercury, cadmium and lead occurred in relatively low concentrations in muscle and organ meats, with the exception of lead in muscle and cadmium in kidneys, which were relatively more contaminated. The concentrations of essential trace metals in samples examined seemed to be natural. Roe-deer contained relatively higher concentrations of copper, both in liver and kidneys, than stag and wild boar, while stag had higher levels of manganese in muscle meat and organs. The weighted mean concentration ranges obtained related to wet-weight for muscle, liver and kidneys of wild boar, roe-deer and stage were 1.2-3.4, 7.3-15, and 24-54 micrograms/kg for mercury; 10-10, 110-210, and 1500-2100 micrograms/kg for cadmium; 86-160, 190-210, and 210-290 micrograms/kg for lead; 1.6 and 1.8, 4.5-28, and 5.4-12 mg/kg for copper; 0.24-0.83, 1.7-5.2, and 1.3-4.1 mg/kg for manganese; 32-37, 37-47 and 30-48 mg/kg for zinc; and 24-31, 40-54, and 67-83 mg/kg for iron, respectively. Single specimens of elk and aurochs were examined also. From the point of view of health, contamination of muscle with lead, as a result of shot pellet fragmentation, and of kidneys with cadmium from the contaminated environment, seemed to be of greatest concern. The values obtained were compared with the available literature data.

Publication Types:
- Review
- Review Literature

PMID: 8178124 [PubMed - indexed for MEDLINE]

1: J Am Coll Nutr 1993 Feb;12(1):31-5

The relationship between placental cadmium, zinc, and copper.

Kuhnert BR, Kuhnert PM, Lazebnik N, Erhard P.

Department of Obstetrics and Gynecology, MetroHealth Medical Center, Cleveland, OH.

A number of interactions between the essential metals zinc (Zn) and copper (Cu), and the toxic metal cadmium (Cd), have been described in animal, but not in human tissues. The purpose of this study was to determine whether Cd levels are directly related to Zn or Cu levels in the human placenta at term, and whether this relationship is affected by parity or smoking. Atomic absorption spectroscopy was used to determine Cd, Zn and Cu in perfused placental cotyledons from 292 low-risk parturients. Plasma thiocyanate levels were used to determine smoking status. Linear regression and repeated measures analysis of variance (ANOVA) were used to examine relationships between the elements and the effects of parity and smoking status. Results show significant correlations between placental Cd and both Zn (r-0.41; $p < 0.01$) and Cu (r-0.35; $p < 0.01$), but only in multiparous patients. These relationships were not altered by smoking. These results suggest that Cd-Zn and Cd-Cu interactions occur in the placenta at "normal" levels of Cd exposure and over a very short time period.

PMID: 8440815 [PubMed - indexed for MEDLINE]

1: Arh Hig Rada Toksikol 1995 Sep;46(3):333-45 Related Articles, Links

The toxicity/essentiality of dietary minerals. A review on some micronutrients prepared in honor of the Award for Life Achievement to Doctor Krista Kostial.

Katz SA.

Rutgers University, Camden, USA.

Continued progress in the theory and practice of trace element analytical chemistry has made possible significant advances in investigating the role and fate of trace elements in biological systems. Public health commissions and environmental protection agencies have subsequently established requirements for intakes of and exposures to trace elements both from the nutritional (copper-zinc) and from the toxicological (cadmium-mercury) perspectives. Some trace elements demonstrate the properties of both categories, and consequently give rise to questions about the toxicity of essential dietary minerals. Selenium and chromium are typical examples of this toxicity-essentiality paradox. The systemic intoxication by and/or nutritional importance of these elements are reviewed as are the criteria for assessing their toxicity and essentiality.

PMID: 8645120 [PubMed - indexed for MEDLINE]

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1: Eur J Appl Physiol Occup Physiol 1996;73(3-4):299-303 Related Articles, Link:

Evaluation of the influence of physical activity on the plasma concentrations of several trace metals.

Rodriguez Tuya I, Pinilla Gil E, Maynar Marino M, Garcia-Monco Carra RM, Sanchez Misiego A.

Departamento de Quimica Analitica y Electroquimica, Universidad de Extremadura, Badajoz, Spain.

Our study was carried out with the aim of evaluating the influence that the degree of physical activity may have on plasma concentrations of essential and toxic elements. Copper and zinc, elements of known importance in basic cellular processes, have been analysed as essential, and cadmium and lead as toxic for the body in abnormal doses. The study was performed on a total population of 50 healthy individuals, 34 of them professional sportsmen and the rest who undertook moderate physical activity (control group), all of them living in a polluted environment (Madrid, Spain). Sampling was conducted at the beginning of the season (October). Electro-analytical techniques of proved reliability and accuracy were used for the determination of the metals. The results were related to data obtained using graphite furnace atomic absorption spectrophotometry and by use of biological reference materials. We found significantly higher zinc plasma concentrations in the sportsmen involved in anaerobic-type training (judo, fencing) compared to those undertaking aerobic activities (endurance, cycling) ($P < 0.05$). The values in both cases were higher than those found in the control group. Our study showed an increase of plasma copper concentrations in professional sportsmen, especially in those performing anaerobic activities, compared to those subjects undertaking moderate activity (control group) ($P < 0.05$). In summary, our results showed that there were no deficiencies of copper and zinc in the athletes studied at the beginning of the season. The levels were higher than those of the control population. As for the toxic metals, cadmium and lead, we observed lower levels in the athletes than in the control group (cadmium $P < 0.005$, lead $P < 0.05$). These results may indicate the existence of possible elimination systems for these metals in athletes, when they are training in a polluted environment.

PMID: 8781860 [PubMed - indexed for MEDLINE]

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Apr 28 2003 10:05:4

1: World Health Stat Q 1997;50(1-2):132-49

Monitoring and assessment of dietary exposure to chemical contaminants.

Baht RV, Moy GG.

National Institute of Nutrition, Hyderabad, India.

The results of the Global Environment Monitoring System/Food Contamination Monitoring and Assessment Programme (GEMS/Food) and other monitoring programmes for priority contaminants in the diet, including lead, cadmium, mercury, polychlorinated biphenyls, organochlorine and organophosphorus pesticide residues and aflatoxin, are presented. These results are assessed with respect to established acceptable or tolerable intakes for these contaminants. While the assessments generally confirm the effectiveness of government efforts to prevent or reduce food contamination in industrialized countries, better exposure estimates for infants and children and other vulnerable groups should be calculated. In developing countries, little reliable information is available on the occurrence of food contamination. Without such information, the health of hundreds of millions of people may be threatened. For these countries, and especially those that employ older agricultural and industrial technologies, basic food contamination monitoring and assessment programmes should be established for at least those contaminants of priority concern. These programmes form an essential basis for developing effective intervention strategies and for efficient management of health and environment resources. In all countries, accidental and sporadic contamination is an ever present danger and continual vigilance is necessary to protect public health. All countries should identify institutions with the analytical capability to support epidemiological investigations of outbreaks of disease that may be associated with consumption of chemically contaminated food. All countries should participate in GEMS/Food to promote health-oriented, population-based monitoring at the national level.

Publication Types:
- Review
- Review, Tutorial

PMID: 9282396 [PubMed - indexed for MEDLINE]

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Apr 28 2003 10:05:4

1: Hum Exp Toxicol 1997 Aug;16(8):429-34 Related Articles, Links

Small-intestinal absorption of cadmium and the significance of mucosal metallothionein.

Elsenhans B, Strugala GJ, Schafer SG.

Walther-Straub-Institut fur Pharmakologie und Toxikologie, Ludwig-Maximilians-Universitat Munchen, Germany.

1 Although food intake is among the most important routes of Cd exposure, not many details are known about the intestinal absorption mechanisms of Cd. In this respect Cd is representative of most other nonessential, merely toxic metals. 2 Based on a concept of two distinguishable steps, intestinal absorption of Cd is characterized by high accumulation within the intestinal mucosa and a low rate of diffusive transfer into the organism. 3 After uptake into the mammalian organism, Cd is sequestered into hepatic metallothionein (MT). It is assumed that hepatic Cd-MT then gradually redistributes Cd to the kidney, which is the main target organ for chronic Cd toxicity. 4 When feeding low levels of dietary CdCl2, however, Cd accumulates preferentially in the kidney and to a lesser degree in the liver, a distribution pattern also found after intravenous and peroral administration of the Cd-MT complex itself. As dietary Cd induces intestinal MT, intestinal Cd-MT complexes could be at least partly responsible for the renal accumulation of dietary Cd. 5 For this mechanism, however, serosal release of mucosal Cd-MT is required. In fact, in vitro findings in rats reveal a concentration-dependent release of intestinal MT to the serosal side of the small intestine. These results indicate that endogenous intestinal MT may deliver Cd-MT to other inner organs, thus contributing to the preferential renal accumulation of ingested Cd.

Publication Types:
- Review
- Review, Tutorial

PMID: 9292282 [PubMed - indexed for MEDLINE]

1: J Trace Elem Med Biol 1997 Nov;11(3):129-36 Related Articles, Links

Determination of various nutrients and toxic elements in different Brazilian regional diets by neutron activation analysis.

Favaro DI, Hui ML, Cozzolino SM, Maihara VA, Armelin MJ, Vasconcellos MB, Yuyama LK, Boaventura GT, Tramonte VL.

Instituto de Pesquisas Energeticas e Nucleares, Comissao Nacional de Energia Nuclear/SP-CP 11049, CEP 05422-970, Sao Paulo, Brazil.

The concentration of 19 elements (As, Br, Ca, Cd, Cl, Co, Cr, Cu, Fe, Hg, K, Mg, Mn, Na, Rb, Sb, Sc, Se and Zn) was evaluated in some diets taken from different regions of Brazil by Instrumental and Radiochemical Neutron Activation Analysis. Several populations with different socio-economic living conditions and inhabiting in different regions of Brazil were studied in order to estimate and to detect the variability of the mineral and toxic element content among Brazilian populational groups. The data obtained showed a significant difference between the contents of these elements in the diets from the regions studied. The general conclusions from the data obtained in this study were: 1) regarding the daily amounts of essential elements (Ca, Cl, Co, Fe, Mn, Na, K, Fe, Se and Zn), the Santa Catarina 2 diet showed the closest values when compared to the recommended values of RDA (Recommended Dietary Allowance) and/or WHO (World Health Organization). The Santa Catarina 1(low income groups) showed the lowest when compared to the same values. 2) The intake of toxic elements (As, Br, Cd, Hg, Sb) among the diets does not seem to be a major problem when compared to PTWI (Provisional Tolerable Weekly Intake, WHO), except for Hg intakes in regions near gold mining activities, like Manaus and Mato Grosso, where the values found were near the upper limit set by WHO.

PMID: 9442457 [PubMed - indexed for MEDLINE]

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1: Environ Health Perspect 1998 Feb;106 Suppl 1:203-16 Related Articles, Link:

Effects of micronutrients on metal toxicity.

Peraza MA, Ayala-Fierro F, Barber DS, Casarez E, Rael LT.

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peraza@toxic.pharm.arizona.edu

There is growing evidence that micronutrient intake has a significant effect on the toxicity and carcinogenesis caused by various chemicals. This paper examines the effect of micronutrient status on the toxicity of four nonessential metals: cadmium, lead, mercury, and arsenic. Unfortunately, few studies have directly examined the effect of dietary deficiency or supplementation on metal toxicity. More commonly, the effect of dietary alteration must be deduced from the results of mechanistic studies. We have chosen to separate the effect of micronutrients on toxic metals into three classes: interaction between essential micronutrients and toxic metals during uptake, binding, and excretion; influence of micronutrients on the metabolism of toxic metals; and effect of micronutrients on secondary toxic effects of metals. Based on data from mechanistic studies, the ability of micronutrients to modulate the toxicity of metals is indisputable. Micronutrients interact with toxic metals at several points in the body: absorption and excretion of toxic metals; transport of metals in the body; binding to target proteins; metabolism and sequestration of toxic metals; and finally, in secondary mechanisms of toxicity such as oxidative stress. Therefore, people eating a diet deficient in micronutrients will be predisposed to toxicity from nonessential metals.

Publication Types:
- Review
- Review, Tutorial

PMID: 9539014 [PubMed - indexed for MEDLINE]

1: Am J Clin Nutr 1998 May;67(5 Suppl):1091S-1097S Related Articles, Links

Mechanisms for protection against copper toxicity.

Dameron CT, Harrison MD.

National Research Centre for Environmental Toxicology, Queensland, Coopers Plains, Australia. c.dameron@mailbox.uq.oz.au

Essential transition metals such as copper, molybdenum, and zinc and nonessential metals like cadmium, mercury, and lead can be toxic at the cellular, tissue, and organ levels when present in excess. To avoid metal-induced toxicity most organisms use a redundant combination of metal-regulated import inhibition, sequestration, and enhanced export mechanisms Combinations of these mechanisms are used to form detoxification pathways controlled through metal-binding proteins at transcriptional, translational, or enzymatic levels. In mammalian pathways copper is partially detoxified by sequestration in the metal-binding metallothioneins or export via the copper-translocating ATPases. Copper regulation of these two mechanisms is afforded by specific conformational changes induced in regulatory proteins on metal binding.

Publication Types:
- Review
- Review, Tutorial

PMID: 9587158 [PubMed - indexed for MEDLINE]

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1: Semin Nephrol 1998 May;18(3):280-94

The mineral disorders in pediatrics.

Linshaw M, Aigbe M, Kaskel F.

Department of Pediatric Nephrology, Floating Hospital for Infants and Children, NEMC, Boston, MA 02111, USA.

There is increasing awareness of the role that metals/minerals play in health and disease. Minerals contribute in essential ways to the fundamental biochemical and physiological functions of cells. Deficit of an essential mineral leads to aberrations in cell function. Alternatively, minerals in excess have significant toxicity, and in an era of increasing threat to a safe environment, the potential for toxic tissue injury to contribute to progressive renal insufficiency and ultimately to unexplained renal failure remains a major concern. This review provides information on selected minerals that are attracting growing attention with respect to their influence on renal function in health and disease. Although all minerals have the potential to cause toxicity if consumed in sufficient quantity, most are essential nutrients whose deficiency is associated with significant health problems. Certain minerals, including aluminum, arsenic, cadmium, lead, and mercury are considered toxic. Their suggested positive effects on the health of animals has been recently summarized, but in humans they are not currently known to exert any clearly beneficial biological or biochemical effect.

Publication Types:
- Review
- Review, Tutorial

PMID: 9613869 [PubMed - indexed for MEDLINE]

1: Ecotoxicol Environ Saf 1998 Oct;41(2):130-6

ELSEVIER SCIENCE FULL-TEXT ARTICLE

Related Articles, Links

Accumulation of cadmium in and its effect on bank vole tissues after chronic exposure.

Swiergosz R, Zakrzewska M, Sawicka-Kapusta K, Bacia K, Janowska I.

Department of Animal Ecology, Jagiellonian University, Ingardena 6, Krakow, 30-060, Poland.

Cadmium is one of many metals that are not physiologically or biochemically essential to organisms. This element is extremely dangerous as it is easily absorbed and remains in tissues for a long time. Long exposure to high doses of cadmium may cause biochemical and functional changes in some critical organs. In this study, wheat grains contaminated with cadmium chloride were used to test the influence of cadmium on male bank voles (Clethrionomys glareolus). Doses used in the experiment were environmentally realistic: 0.25 microg g-1 (control), 15 microg g-1, and 40 microg g-1 cadmium (dry weight). The animals were given cadmium-contaminated food and clean water ad libitum for 3 and 6 months. After these exposures, the animals were killed and the kidneys, liver, and testes from each vole were collected for analyses. The concentrations of Cd, Cu, Zn, and Fe in the tissues were determined with an atomic absorption spectrophotometer. The formalin-fixed testes, kidneys, and part of the liver were embedded in paraffin and then stained with hematoxylin and eosin. Cadmium accumulation in the tissues was directly proportional to dose. The highest cadmium concentrations were found in the kidneys of animals fed the highest dose of cadmium. Histological examination of the tissues revealed some pathological changes in the structure of kidneys, liver, and testes.

PMID: 9756701 [PubMed - indexed for MEDLINE]

1: Tierarztl Prax Ausg G Grosstiere Nutztiere 1998 Sep;26 (5):269-75

[Disturbances in the status of trace elements in cattle from the point of view of herd supervision. 2: New trace elements]

[Article in German]

Gelfert CC, Staufenbiel R.

Klinik fur Klauentiere, Freien Universitat Berlin.

In this bipartite article the current knowledge about trace elements in cattle is reviewed. The second part contains the new trace elements. This group includes the essential elements arsenic, lead, nickel, vanadium, tin, silicon and the accidental elements. Of the last aluminum, boron, cadmium, mercury and thallium have an importance for cattle due to their toxic potential and the risk of contamination of the food originating from the animal.

PMID: 9810605 [PubMed - indexed for MEDLINE]

1: Mutat Res 1999 Feb 19;439(2):301-6

DNA damage produced by cadmium in a human fetal hepatic cell line.

Lopez-Ortal P, Souza V, Bucio L, Gonzalez E, Gutierrez-Ruiz MC.

Laboratorio de Fisiologia Celular, Departamento de Ciencias de la Salud, Division de Ciencias Biologicas y de la Salud, Universidad Autonoma Metropolitana-Iztapalapa, Apdo Postal 55-535, Mexico, D.F. 09340, Mexico.

Cadmium (Cd) is one of the most important heavy metal environmental toxicants. It alters a wide variety of cellular and biochemical processes. The objective of this work was to study DNA damage and recovery after acute and chronic CdCl2 treatment in a human fetal hepatic cell line (WRL-68 cells). Using the alkaline microgel electrophoresis assay that detects DNA single-strand breaks and/or alkali-labile sites in individual cells, we evaluatec for levels of DNA damage. The mean migration length in control cells was 35.37+/-1. 43 microm (8% damaged cells), whereas the mean migration in cells treated with 0.005 microM CdCl2 for 3 h (acute low dose) was 65. 87+/-2.07 microm (88% damaged cells). Treatment with 0.01 microM CdCl2 for the same time (acute high dose) increased the mean migration length to 125.79+/-2.91 microm (92% damaged cells). However, a 0.005 microM CdCl2 treatment for 7 days (chronic treatment) only increased 65% DNA migration to 58.38+/-2.59 microm (88% damaged nucleus). Lipoperoxidative damage expressed as malondialdehyde (MDA) production per milligram of protein was 15. 7+/-2.6 for control cells, whereas in Cd-treated cells the values were 20.2+/-2.4 (acute low dose), 22.9+/-2.2 (acute high dose), and 22.6+/-2.1 (chronic treatment). To study the repair of DNA damage, cells were washed with 0.01 microM meso-2,3-dimercaptosuccinic acid (DMSA), and fresh Dulbecco's modified essential medium (DMEM) added. The percentage of damaged cells diminished after 90 min, with DNA migration returning to control values by 120 min. Cd treatment produced DNA single-strand breaks and the damage was greater in acute high dose treated cells. Lipid peroxidation values did not correlate with DNA single-strand breaks.

PMID: 10023089 [PubMed - indexed for MEDLINE]

1: Eur J Clin Nutr 1999 Jun;53(6):486-94

Trace element transfer from the mother to the newborn--investigations on triplets of colostrum, maternal and umbilical cord sera.

Krachler M, Rossipal E, Micetic-Turk D.

Institute for Analytical Chemistry, Karl-Franzens-Universitat Graz, Austria.

OBJECTIVE: To investigate the trace element transfer from the mother to the newborn. DESIGN: The concentrations of the eight essential elements calcium (Ca), cobalt (Co), copper (Cu), magnesium (Mg), manganese (Mn), molybdenum (Mo), tin (Sn), and zinc (Zn), and of the non-essential and toxic elements barium (Ba), beryllium (Be), bismuth (Bi), cadmium (Cd), cesium (Cs), lanthanum (La), lithium (Li), lead (Pb), rubidium (Rb), antimony (Sb), strontium (Sr), and thallium (Tl) were determined in umbilical cord (n = 29) and corresponding maternal sera (n = 29) as well as in colostrum (n = 27). RESULTS: Umbilical cord serum concentrations of Ca, Mn, and Zn were 120%, 150%, and 148% of the maternal value, respectively. Maternal sera had twice the Cu concentrations found in healthy adults and five-times higher Cu than umbilical cord sera. Concentration ratios colostrum/maternal serum and colostrum/umbilical cord serum were approximately one for Co, 1.4 for Mg, two for Ca, Mn, and Sn, five for Cu (maternal serum), eight for Mo, and ten for Zn. Concentrations of the toxic elements Cd and Pb decreased in the order colostrum (Pb 2.6 microg/L; Cd 0.6 microg/L), maternal sera (0.8 microg/L; 0.3 microg/L), umbilical cord sera (0.4 microg/L; 0.2 microg/L). Maternal serum Ba and Rb was 182% and 66% of the umbilical cord value. For Sr and Li, an almost perfect correlation between umbilical cord and maternal sera was found. For Ba, Co, Cu, Mn, Zn none, and for Ca, Cs, Mn, Mo, Rb only weak positive correlations between these two compartments could be established. CONCLUSIONS: The results of this study indicate that an active transport mechanism for the transport of Ca, Mn, Rb, and Zn from the mother to the newborn exists, whereas Cs, Li, and Sr follow concentration gradients. As regards Cu, the placenta showed to have a blocking effect on the transfer from the mother to the baby.

PMID: 10403586 [PubMed - indexed for MEDLINE]

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Apr 28 2003 10:05:4

1: Cancer Epidemiol Biomarkers Prev 2000 Feb;9(2):139-45

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Is cadmium a cause of human pancreatic cancer?

Schwartz GG, Reis IM.

Department of Cancer Biology and Public Health Sciences, Comprehensive Cancer Center of Wake Forest University, Winston-Salem, North Carolina 27157, USA. gschwart@wfubmc.edu

Little is known about the etiology of pancreatic cancer, which is an important cause of cancer mortality in developed countries. We hypothesize that exposure to cadmium is a cause of pancreatic cancer. Cadmium is a nonessential metal that is known to accumulate in the human pancreas. The major risk factors for pancreatic cancer (increasing age, cigarette smoking, residence in Louisiana, and occupations involving exposure to metalworking and pesticides) are all associated with increased exposure to cadmium. Our meta-analysis of cohorts with high exposure to cadmium is also consistent with an increased risk of pancreatic cancer (standardized mortality ratio = 166; 95% confidence interval, 98-280; P = 0.059). Cadmium can cause the transdifferentiation of pancreatic cells, increases in the synthesis of pancreatic DNA, and increases in oncogene activation. Thus, cadmium is a plausible pancreatic carcinogen. The cadmium hypothesis provides a coherent explanation for much of the descriptive epidemiology of pancreatic cancer and suggests new avenues for analytical research.

Publication Types:
- Meta-Analysis

PMID: 10698473 [PubMed - indexed for MEDLINE]

1: Proc Natl Acad Sci U S A 2000 Apr 25;97(9):4991-6

Cadmium and iron transport by members of a plant metal transporter family in Arabidopsis with homology to Nramp genes.

Thomine S, Wang R, Ward JM, Crawford NM, Schroeder JI.

Department of Biology and Center for Molecular Genetics, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0116, USA.

Metal cation homeostasis is essential for plant nutrition and resistance to toxic heavy metals. Many plant metal transporters remain to be identified at the molecular level. In the present study, we have isolated AtNramp cDNAs from Arabidopsis and show that these genes complement the phenotype of a metal uptake deficient yeast strain, smf1. AtNramps show homology to the Nramp gene family in bacteria, yeast, plants, and animals. Expression of AtNramp cDNAs increases Cd(2+) sensitivity and Cd(2+) accumulation in yeast. Furthermore, AtNramp3 and AtNramp4 complement an iron uptake mutant in yeast. This suggests possible roles in iron transport in plants and reveals heterogeneity in the functional properties of Nramp transporters. In Arabidopsis, AtNramps are expressed in both roots and aerial parts under metal replete conditions. Interestingly, AtNramp3 and AtNramp4 are induced by iron starvation. Disruption of the AtNramp3 gene leads to slightly enhanced cadmium resistance of root growth. Furthermore, overexpression of AtNramp3 results in cadmium hypersensitivity of Arabidopsis root growth and increased accumulation of Fe, on Cd(2+) treatment. Our results show that Nramp genes in plants encode metal transporters and that AtNramps transport both the metal nutrient Fe and the toxic metal cadmium.

PMID: 10781110 [PubMed - indexed for MEDLINE]

1: Food Addit Contam 2000 Jan;17(1):45-53

Trace metals in soft and durum wheat from Italy.

Conti ME, Cubadda F, Carcea M.

Dipartimento di Controllo e Gestione delle Merci e del loro Impatto sull'Ambiente, Universita di Roma La Sapienza, Italy.

A survey was carried out with the aim to assess the levels of some toxic (cadmium, lead) and essential (copper, zinc) trace metals in wheat grown in Italy. A total of 178 samples of soft wheat grain and 239 samples of durum wheat grain from all the Italian wheat-growing regions were pooled into 35 and 38 representative samples respectively. After dry ashing, cadmium and lead were determined by graphite furnace atomic absorption spectrometry (GFAAS), whereas copper and zinc were determined by flame atomic absorption spectrometry (FAAS). In soft wheat the mean and median contents of all samples were (on a dry weight basis) 40 and 33 micrograms kg-1 for cadmium, 16 and 14 micrograms kg-1 for lead, 3.4 and 3.2 mg kg-1 for copper, 33 and 32 mg kg-1 for zinc. Similar levels were found in durum wheat. In this latter case the mean and median were 42 and 39 micrograms kg-1 for cadmium, 15 and 14 micrograms kg-1 for lead, 3.5 and 3.2 mg kg-1 for copper, 34 and 34 mg kg-1 for zinc. Significant differences were detected for some metals in relation to geographical provenance and variety. The average intake of the four selected elements from wheat-based products was estimated for the Italian population.

PMID: 10793853 [PubMed - indexed for MEDLINE]

1: Biofactors 2000;11(3):149-62

Is chromium a trace essential metal?

Stearns DM.

Northern Arizona University, Department of Chemistry, Flagstaff 86011-5698, USA. Diane.Stearns@nau.edu

If chromium is an essential metal it must have a specific role in an enzyme or cofactor, and a deficiency should produce a disease or impairment of function. To date, no chromium-containing glucose tolerance factor has been characterized, the purpose of the low-molecular-weight chromium-binding protein is questionable, and no direct interaction between chromium and insulin has been found. Furthermore, chromium3+ is treated like the toxic metals arsenic, cadmium, lead and mercury in animals. Chromium3+ may be involved in chromium6+-induced cancers because chromium6+ is converted to chromium3+ in vivo, and chromium3+ is genotoxic and mutagenic. Although there is no direct evidence of chromium deficiencies in humans, dietary supplements exist to provide supraphysiological doses of absorbable chromium3+. Chromium3+ may act clinically by interfering with iron absorption, decreasing the high iron stores that are linked to diabetes and heart disease. If so, this would make chromium3+ a pharmacological agent, not an essential metal.

Publication Types:
- Review
- Review, Academic

PMID: 10875302 [PubMed - indexed for MEDLINE]

1: Biol Trace Elem Res 2000 May;74(2):97-105

Seminal plasma trace metal levels in industrial workers.

Dawson EB, Evans DR, Harris WA, Powell LC.

Department of Obstetrics & Gynecology, The University of Texas Medical Branch, Galveston 77555, USA.

This study compares the seminal plasma trace metal levels of hospital workers with groups of industrial workers in a petroleum refinery, smelter, and chemical plant. The metals measured were the essential metals (copper, zinc, nickel, cobalt, and manganese) and the toxic metals (lead, cadmium, and aluminum). The group mean +/- SE metal level for each group (50 subjects per group) was calculated, and the statistical significance of the group mean differences of the industrial groups with the hospital group (control) was determined by the Student's t-test. The differences observed in the smelter group were increased copper and zinc ($p < or = 0.001$) and decreased nickel, cobalt, and manganese ($p < or = 0.001$, $< or = 0.01$). The refinery group differences were increased copper, zinc, and nickel ($p < or = 0.001$) but decreased cobalt and manganese ($p < or = 0.001$). The chemical group differences were increased zinc ($p < or = 0.001$) and decreased cobalt ($p < or = 0.001$). The seminal plasma levels of the toxic metals lead and aluminum were increased in each of the industrial groups ($p < or = 0.001$). Concurrent differences were (1) decreased accumulation of nickel, cobalt, and manganese in the smelter group, (2) decreased cobalt and manganese in the refinery group, and (3) only decreased cobalt in the chemical group.

Publication Types:
- Clinical Trial

PMID: 11051584 [PubMed - indexed for MEDLINE]

1: Int J Food Sci Nutr 2001 Jul;52(4):379-82

Cadmium in zinc-containing mineral supplements.

Krone CA, Wyse EJ, Ely JT.

Applied Research Institute, PO Box 1925, Palmerston North, New Zealand.

Seven zinc-containing dietary supplements were analyzed for zinc (Zn) and cadmium (Cd) by inductively coupled plasma/mass spectrometry (ICP/MS). Cadmium was detected in all samples; however, the amount of Cd per 15 mg Zn (the daily US Recommended Dietary Allowance) varied by over 37-fold (0.039 to 1.46 micrograms Cd/15 mg Zn). Supplements with Zn in the form of a gluconate consistently contained the lowest amounts of Cd. Because Cd is a non-essential potentially toxic element for humans, its concentration in nutritional supplements should be minimized and possibly regulated by government-established standards.

PMID: 11474903 [PubMed - indexed for MEDLINE]

1: In Vitr Mol Toxicol 2001 Spring;14(1):25-42

Metallothionein overexpression in human trophoblastic cells protects against cadmium-induced apoptosis.

McAleer MF, Tuan RS.

Department of Orthopaedic Surgery, Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA.

Proper functioning of trophoblastic cells is essential for maintenance of the placenta and development of the embryo/fetus. Exposure of trophoblasts to toxic exogenous factors, such as cadmium (Cd), perturbs placental function and affects fetal outcome. Cellular responses to Cd exposure include induction of the metal-binding protein, metallothionein (MT), and initiation of apoptosis. To analyze the functional relationship between cellular MT levels and apoptosis in trophoblasts, we have examined the effects of DNA transfection-mediated alterations in MT levels on trophoblastic function and apoptosis, with and without Cd exposure, using the trophoblast-like JEG-3 human choriocarcinoma cell line. JEG-3 cells stably transfected with human MT-IIa cDNA expression constructs, in either sense or antisense orientation, were unchanged in human chorionic gonadotropin (hCG) production or expression of the apoptotic markers, bcl-2 and CPP-32. However, MT overexpression significantly prolonged the recovery time of intracellular Ca flux, whereas reduced basal MT increased the incidence of apoptosis as determined by morphology and terminal deoxynucleotidyl end labeling (TUNEL) staining. Upon Cd exposure, a dose-dependent decrease in hCG secretion was seen in all JEG-3 cultures, without any correlation to basal MT expression. Basal MT levels, however, significantly affected the extent of apoptosis, the incidence being inversely related to basal MT level. These results suggest that while MT does not ameliorate heavy-metal induced perturbation of some trophoblastic functions, its expression is critical for protection of these cells from Cd-induced apoptosis and could act to maintain placental integrity in cases of maternal Cd exposure.

PMID: 11689154 [PubMed - indexed for MEDLINE]

1: Int J Occup Med Environ Health 2001;14(3):223-9

Blood concentration of essential trace elements and heavy metals in workers exposed to lead and cadmium.

Wasowicz W, Gromadzinska J, Rydzynski K.

Department of Toxicology and Carcinogenesis, Nofer Institute of Occupational Medicine, Lodz, Poland.

The aim of the study was to determine blood concentration of essential trace elements (Se, Zn, Cu) and toxic metals (Pb, Cd), markers of antioxidant (activities of glutathione peroxidase (GPx), superoxidase dismutase and ceruloplasmin) and prooxidant processes (thiobarbituric acid reactive substances (TBARS)) in workers exposed to Pb and Cd. Forty three male workers of the lead-acid batteries department, aged 25-52 years, and twenty two workers, including 15 women, aged 36-51 years, exposed to Cd in the alkaline batteries department were examined. The reference group consisted of 52 healthy inhabitants of the same region. It was found that Se concentration and GPx activity in both erythrocytes and plasma of Cd exposed workers were significantly lower ($p < 0.001$) than in the reference group. We found an inverse linear correlation between blood Se and Cd concentrations in the workers exposed to Cd ($r = -0.449$; $p < 0.01$). Moreover, the activity of erythrocyte and plasma GPx was shown to be significantly lower in the study group of workers ($p < 0.001$). It was observed that TBARS concentration in plasma was significantly higher ($p < 0.05$) in the lead exposed workers than in the group without contact with Pb. Our results indicate that exposure to Pb and Cd affects the antioxidant potential of blood in workers exposed to heavy metals.

PMID: 11764849 [PubMed - indexed for MEDLINE]

1: Arch Environ Contam Toxicol 2002 Feb;42(2):165-72

Interactions between toxic and essential trace metals in cattle from a region with low levels of pollution.

Alonso ML, Benedito JL, Miranda M, Castillo C, Hernandez J, Shore RF.

Universidade de Santiago de Compostela, Departamento de Patoloxia Animal, Facultade de Veterinaria, 27002 Lugo, Spain.
mlalonso@lugo.usc.es

Studies on the impacts of pollutant metals and metalloids on livestock have largely focused on animals with relatively high levels of exposure. The impact of low-level environmental contamination, which is more common on agricultural land, is largely unknown. The principal aim of the present study was to examine the effects of low-level environmental contamination on trace metal metabolism in cattle from the rural and relatively uncontaminated region of Galicia (NW Spain). Correlations between toxic (cadmium, lead, and arsenic) and essential trace elements (copper and zinc) were evaluated in the tissues (liver, kidney, and muscle) and blood of 494 cattle from throughout Galicia. Cadmium was the toxic element that had the greatest influence on copper and zinc homeostasis. There was a significant positive association between renal cadmium and zinc residues and a significant negative correlation between kidney cadmium and copper. These interactions are likely to be the result of cadmium-induced effects on metallothionein synthesis. Lead and zinc were positively associated in the kidney, although the mechanism of this interaction is uncertain. Arsenic and copper concentrations were strongly correlated with each other in the liver and may indicate that the high copper levels in animals from copper-rich areas in Galicia interfere with their arsenic excretion. The essential metals copper and zinc were also significantly associated with each other in calves but not in cows.

PMID: 11815807 [PubMed - indexed for MEDLINE]

1: Toxicol Appl Pharmacol 2002 Aug 1;182(3):255-65 Related Articles, Links

ELSEVIER SCIENCE FULL-TEXT ARTICLE

Cadherins and NCAM as potential targets in metal toxicity.

Prozialeck WC, Grunwald GB, Dey PM, Reuhl KR, Parrish AR.

Department of Pharmacology, Midwestern University, Downers Grove, Illinois 60515, USA. wprozi@midwestern.edu

Cell adhesion molecules are cell surface proteins that play critical roles in cell recognition and cell adhesion. These adhesion molecules, which include the cadherins, integrins, occludins, and a variety of immunoglobulin-like molecules, are essential for a wide variety of physiologic processes such as epithelial barrier function, tissue development, learning and memory, and immune responses. In light of the evidence that toxic metals can affect many of these processes, investigators have begun to examine the possibility that cell adhesion molecules may be targets for metal toxicity. This review summarizes the results of recent studies showing that certain cell adhesion molecules, particularly the cadherins family of Ca(2+)-dependent cell adhesion molecules and the immunoglobulin family of Ca(2+)-independent cell adhesion molecules, may be important early targets on which toxic metals such as a Cd, Hg, and Pb act to produce their toxic effects. These metals, and in some cases their organic compounds, can target cell adhesion molecules at multiple levels, including protein-protein interactions, post-translational modification, and transcriptional regulation. Moreover, by interfering with the normal function of the cadherin family of cell adhesion molecules, some of these metals may activate the beta-catenin nuclear signaling pathway. These studies have provided important new insights into the molecular mechanisms of metal toxicity and have opened several exciting avenues of research.

Publication Types:

- Review
- Review, Tutorial

PMID: 12183105 [PubMed - indexed for MEDLINE]

1: Environ Health Perspect 2002 Oct;110 Suppl 5:793-5 Related Articles, Links

Available at ehp Online

The prospective role of abnormal methyl metabolism in cadmium toxicity.

Poirier LA, Vlasova TI.

National Center for Toxicological Research, Food and Drug Administration Jefferson, AR 72079, USA. LPOIRIER@nctr.fda.gov

Several lines of evidence point to the probable role of abnormal methylation processes in the toxicology of metals and other xenobiotics. The spectrum of toxic effects exhibited by such metals as Ni, As, and Cd, as well as by Zn deficiency, often resemble those seen in animals chronically fed methyl-deficient diets. These metal-associated pathologies include cancer, atherosclerosis, birth defects, neurological disturbances, and pancreatic lesions. In addition, each of the above agents has been shown to alter normal methyl group metabolism in vivo or in vitro. In the present studies, we compared the effects on the enzyme DNA methyltransferase (MTase) of two metal ions: the essential metal Zn and the carcinogen Cd. MTase extracts were obtained from the hepatic nuclei of rats fed a methyl-deficient diet (lacking choline and folate) for 7 and 24 weeks. Control animals were fed the same diet supplemented with each of these vitamins. Zn and Cd both inhibited MTase in the nuclear extracts from both the control and the methyl-deficient rats. The inhibitory activity of Cd was greater than that of Zn regardless of whether the nuclear extracts were from the control or the deficient animals. In addition, the kinetics of Cd inhibition of MTase activity were different in the nuclear extracts from the control and methyl-deficient rats. The results provide evidence that the carcinogenic effects of Cd may be mediated in part through abnormal DNA methylation.

PMID: 12426133 [PubMed - indexed for MEDLINE]

1: Toxicol Lett 2003 Jan 31;137(1-2):65-83

Related Articles, Links

ELSEVIER SCIENCE FULL-TEXT ARTICLE

A global perspective on cadmium pollution and toxicity in non-occupationally exposed population.

Satarug S, Baker JR, Urbenjapol S, Haswell-Elkins M, Reilly PE, Williams DJ, Moore MR.

National Research Centre for Environmental Toxicology, University of Queensland, 39 Kessels Road, Coopers Plains, Qld 4108, Brisbane, Australia.

Cadmium is a non-essential element that has high rates of soil to plant transference compared with other non-essential elements, and certain plant species accumulate large amounts of cadmium from low cadmium content soils. In this paper, levels of cadmium found in major food groups are highlighted together with cadmium levels found in liver and kidney samples from non-occupationally exposed populations. Data on human kidney cadmium levels identified recently, including the study in our own laboratory, are compared with older studies. Human-tissue cadmium contents showed large variations among individuals, but sources of the variation remain unknown. Exposure levels of 30-50 microg per day have been estimated for adults and these levels have been linked to increased risk of bone fracture, cancer, kidney dysfunction and hypertension. Increased mortality was found among individuals showing signs of cadmium renal toxicity compared with those without such signs, suggesting that renal toxicity may be an early warning of complications, sub-clinical or clinical morbidity.

Publication Types:

- Review
- Review, Academic

PMID: 12505433 [PubMed - indexed for MEDLINE]

1: Environ Sci Technol 2002 Dec 15;36(24):5363-8

Reduced Cd accumulation in Zea mays: a protective role for phytosiderophores?

Hill KA, Lion LW, Ahner BA.

School of Civil and Environmental Engineering, Cornell University, Ithaca, New York 14853, USA.

Cadmium is a nonessential trace metal and a frequent soil contaminant. Because plants vary in their accumulation of Cd, an understanding of the specific processes that control uptake could reveal methods for reducing Cd levels in edible plant tissues and conversely increasing Cd accumulation in plants used for phytoremediation. Phytosiderophores are iron chelators excreted by graminaceous plants under conditions of iron limitation, but they also complex other metals including cadmium. Here we examine the influence of Cd exposure on phytosiderophore production by hydroponically grown maize. Cd increased the rate of the phytosiderophore 2'-deoxymugineic acid (DMA) release under both Fe-sufficient and Fe-limiting conditions (+/-Fe). In addition, the -Fe plants released more DMA while taking up less Cd than the +Fe plants. In other short-term Cd uptake experiments, plants exposed to Cd in the presence of root exudates in which the DMA-Cd complex was likely the dominant Cd species displayed reduced Cd accumulation in root tissue, and plants similarly exposed to strongly chelated Cd in the presence of EDTA (employed as a positive control) contained the least Cd. Collectively, these results indicate that Cd stress causes Fe deficiency symptoms that result in greater DMA production by maize roots, and then the DMA appears to reduce Cd accumulation.

PMID: 12521162 [PubMed - in process]